Page 4, line 25, please delete "cyclopenantophenanthrene" and insert -- cyclopentanophenanthrene--.

Page 4, line 29, please delete "diasteromers" and insert -- diastereomers--.

Page 5, line 12, replace "diesteromer" with --diastereomer --.

Page 7 line 26, replace "hyopoxia" with --hypoxia--.

Page 8, line 5, replace "dysrhymias, artrial" with --dysrhythmias, arterial--.

Page 8, line 9, replace "emphysemia" with --emphysema--.

Page 8, line 12, replace "glomeruloneprítis" with --glomerulonephritis--.

REMARKS

Claims 1-11 are currently pending in the application.

The Pending Claims Are Non-Obvious In View Of Simpkins '601

All pending claims are rejected as obvious and therefore unpatentable over Simpkins et al. (US Patent No. 5,554,601). The pending claims are also rejected under the judicially created doctrine of obviousness-type double patenting. Applicant traverses these related rejections and requests reconsideration and allowance.

Claim 1 is directed to a novel compound, having cytoprotective properties and comprising a polycyclic compound having from 2-4 carbon rings, and having a phenol group at a first end and an alkylether-substituted terminal carbon ring at its other end, the alkylether portion of the functional group having a formula C_nH_{2n+2} wherein n is at least 3 and less than 20. Claims 2-11 are either dependent upon claim 1 or are substantially

similar but of narrower scope, and hence the following discussion should be seen as applicable to those claims as well.

"[T]he doctrine of obviousness-type double patenting rejects application claims to subject matter different **but not patentably distinct** from the subject matter claimed in a prior art patent," *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993). The Goodman court went on to elaborate the two necessary inquiries for determining double patenting: (a) same invention, i.e. are the claims of identical scope (invoking 35 USC § 101) or (b) are the claims a merely obvious variation.

A similar analysis was followed in a slightly earlier, perhaps more on point, decision, *Ortho Pharmaceutical Corp. v. Smith*, 959 F.2d 936, 22 USPQ2d 1119 (Fed. Cir. 1992), in which a patent challenger failed to show obviousness-type double patenting. In that case, as here, steroid compounds (gon-4-enes) were not mere obvious variations of the prior art steroid compounds gon-5-enes, gon-5(10)-enes and gona-2,5(10)-dienes. The CAFC found that the trial court had properly found no suggestion in the prior art (and hence it could not be obvious) to modify the prior art to achieve the new claimed compounds having the old properties of the prior art compounds and that the level of predictability in the art at the time would not have led one to reasonably predict the effect of the small structural changes in the prior art compounds.

A. The Scope Of The Claims Are Vastly Different

Now turning to a comparison of the claims of the cited reference with the invention claimed herein. The '601 patent claims a **method** comprising the administration of **estrogen** compounds for conferring neuroprotection on a population of

cell. In claim 2 of the reference, the claim is further narrowed to a method for conferring neuroprotection by administering a particular subset of estrogens, namely where the R2 group on C17 is in the α-isomeric position. In claim 4, we have the first mention of a method for conferring neuroprotection by administering ether forms of the **α-isomeric** compounds of claim 2, the particular ethers being ethyl ether and benzyl ether. By contrast, claim 1 of the present application claims a cytoprotective compound (not a method) and is not restricted to estrogens but embraces compounds having from 2-4 rings having a terminal phenolic group at one end and a 3-19 carbon length alkyl ether functional group at the other cyclic end. Claim 1 of the present invention is not restricted to α-estrogens, nor does it claim ethylether or benzylether forms of the broader class of 2-4 ring polycyclic compounds, let alone claim such ethers of α-estrogens.

B. The '601 Does Not Suggest (or Obviate) The Claimed Compounds

The second *Goodman* enquiry is whether the claimed invention is a "merely obvious variation" of the first. In this case, it is clear that not only is the invention of claim 1 not a merely obvious variation (and hence is not an example of obviousness-type double patenting) it is also not even obvious enough to sustain a § 103 rejection. As taught in the instant specification, at page 6, lines 15-20, the observed cytoprotective effect is not related to estrogenicity, and was found to apply to many cell types (not just neural cells) whether they carried estrogen receptors or not. Additionally, as noted in the specification, it was surprisingly found that substituting with either too large a functional group or too small a functional group can dramatically affect the compounds cytoprotective abilities. Most surprisingly, it was found that certain exemplary

embodiments can have 10-fold the cytoprotective activity of the underlying estrogenic compounds from which they were derived, as long as the derivative obeys the claimed limitations. None of these insights are disclosed in the cited reference, nor does the cited reference suggest such modifications. In fact, it may be said that the cited reference actually teaches away from the claimed invention since the applicants' comparison of the ethyl ether substituted compound (most similar to the compounds shown in the '601 reference) with the larger alkyl-substituted derivatives shows that the ethyl ether derivative (4a) was not even as cytoprotective as the parent compound (see page 16, line 32). Nothing in the cited reference reveals the complexity of the relationship of cytoprotective properties and 17-alkoxy chain length. Reflecting again upon the *Ortho* decision, *supra*, how much more so are the presently claimed compounds unobvious in view of the cited references since the unobvious modifications actually, and most surprisingly, even improve on the protective effects of the known compounds.

In view of the foregoing remarks, it is believed that obviousness-type rejections, either under 35 USC § 103 or the obviousness-type double patenting, should be reconsidered and withdrawn and the claims should be allowed.

The Claims Are Allowable As Not Indefinite Under 35 USC § 112

The claim term "comprising" is completely appropriate and not indefinite as applied to the claimed **compounds** (not steps, see Page 3, line 20 of the Office Action). Given the discussion in the specification regarding the required interplay between the phenol and the alkylether ends of the polycyclic compounds of the claimed invention, and further given the applicants' discussion regarding enhancing lipophilicity of the

alkylether substituted end, it is clear that further as yet unknown substitution of the claimed compounds may possibly enhance the claimed compounds without exceeding the scope of the claimed core. To limit the applicants' claim to a core of compounds without including simple additional substitutions would permit potential infringers such an easy opportunity to design around the claimed invention as to render the claim valueless and unfairly deprive applicants' of their due reward for adding so substantively to the body of knowledge in the field.

The Office Action continues by asking the meaning of the term "cytoprotective compound", noting that the claims are not method claims (after having faulted the claims for failing to exclude steps in the previous paragraph). The meaning of the term is (a) well known to those of ordinary skill in the art; and (b) is specifically defined in the specification at page 4, line 31 as a measurable positive effect on cell survival.

With respect to the rejection under 35 USC §112 first paragraph, applicant respectfully points out that (a) the incorporated references are replete with compounds, not just estradiol and other steroids, having certain structural characteristics in common and which have been shown to have similar activities within certain, recognized spheres; and (b) the claims are not directed to "estradiol and other steroid containing A as aromatic ring" but to 2-4 ring compounds having a terminal **phenol** group and having a substituted alkylether cyclic at the other end, where the alkylether is from 3 to 19 carbons in length. Applicants are justified, based on the disclosed exemplary embodiments and further on their existing work showing certain structure-to-activity relationships in a variety of 2-4 ring polycyclic phenolic compounds as shown in the incorporated references US patents 5,859,001, 5,554,601 and 6,197,833, to characterize their invention

as being enabled with respect to the claimed class of compound and the parent compounds indicated.

In view of the foregoing remarks, it is believed that all of the outstanding rejections should be reconsidered and withdrawn and applicants respectfully request allowance of the application.

Miscellaneous Matters

The Applicant has taken this opportunity to make minor amendments, mostly in the nature of typographical errors. No new subject matter has been added by the amendments.

CONCLUSION

For the reasons set forth above, it is respectfully submitted that all pending claims are in condition for allowance. Reconsideration of the claims and a notice of allowance are therefore requested.

Applicant respectfully urges the Examiner to accept a phone interview should continued rejection be contemplated. Applicant will contact the Examiner for the purpose of arranging such an interview within the week following the filing of this Response.

Applicant has submitted herewith a Petition for 1 Month Extension of the Shortened Non-Statutory Time For Response. In the event it is believed that a greater extension of time is needed, the Commissioner is authorized to charge deposit account

number 19-4972 for any additional fees that may be required for the timely consideration of this application.

Date: November 4, 2002

Respectfully submitted,

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